

What is claimed is:

1. A system for use in detecting biological material of a biological sample, the system
5 comprising:

a positioning apparatus for providing a biological sample in a sampling position, wherein
the biological sample comprises biological material associated with a biological material holding
structure, the biological material holding structure having first and second opposing sides;

10 an electronic light detector array, wherein the electronic light detector array comprises a
plurality of detector pixels located at particular detector pixel addresses, and further wherein the
plurality of detector pixels faces the first side of the biological sample to receive light therefrom;
and

15 a light source operable to provide source light, wherein the sampling position is a
position that places the biological sample in a defined spatial relationship relative to the
electronic light detector array such that the source light impinges on at least one portion of the
first side of the biological material holding structure of the biological sample, and further such
that, in response to such impinging light, light representative of the biological sample is provided
via a light path for detection by one or more of the detector pixels; and

20 control circuitry operable to acquire at least one frame of image data representative of
biological material of the biological sample using the plurality of detector pixels to detect the
light representative of the biological sample provided via the light path.

- 25 2. The system of claim 1, wherein the control circuitry is operable to acquire a plurality of
frames of image data representative of biological material of the biological sample using the
plurality of detector pixels.

3. The system of claim 2, wherein the control circuitry is further operable to provide an
image for display using the plurality of frames of image data.

- 30 4. The system of claim 1, wherein the light source provides an excitation light that impinges

on the at least one portion of the biological material holding structure of the biological sample, and further such that, in response to such excitation light, fluorescence representative of biological material of the biological sample is provided via the light path for detection by one or more of the plurality of detector pixels, and further wherein the control circuitry is operable to acquire at least one frame of image data representative of detected fluorescence.

5. The system of claim 4, wherein the light path of the fluorescence to one or more of the detector pixels does not include any portion of the biological material holding structure.

10. 6. The system of claim 4, wherein the first side of the biological material holding structure comprises a sample surface having biological material thereon, and further wherein the sample surface is facing the plurality of detector pixels.

15. 7. The system of claim 4, wherein the system further comprises an emission light filter positioned between the biological sample and the plurality of detector pixels operable to prevent excitation light from impinging on the plurality of detector pixels.

20. 8. The system of claim 4, wherein the system further comprises a focusing lens positioned between the biological sample and the plurality of detector pixels operable to map the fluorescence onto one or more of the plurality of detector pixels.

25. 9. The system of claim 4, wherein the biological material holding structure comprises an opaque material.

10. 10. The system of claim 4, wherein the light path of the fluorescence to one or more of the detector pixels includes at least a portion of the biological material holding structure.

11. 11. The system of claim 4, wherein the biological sample is one of a micro-array and a gel, and further wherein one or more portions of the biological material of the biological sample comprise fluorescent markers.

12. The system of claim 1, wherein, in response to such impinging light, reflected light representative of the biological sample is provided via the light path for detection by one or more of the plurality of detector pixels, and further wherein the control circuitry is operable to acquire at least one frame of image data representative of detected reflected light.

5

13. The system of claim 12, wherein the first side of the biological material holding structure comprises a sample surface having biological material thereon, and further wherein the sample surface is facing the plurality of detector pixels.

10 14. The system of claim 12, wherein the system further comprises a focusing lens positioned between the biological sample and the plurality of detector pixels operable to focus the reflected light onto one or more of the plurality of detector pixels.

15. The system of claim 12, wherein the biological holding material structure comprises an opaque material.

16. The system of claim 12, wherein the biological sample is one of a micro-array and a gel.

20 17. The system of claim 1, wherein the first side of the biological sample comprises a sample surface of a micro-array having one or more sequences of nucleic acids immobilized thereto, each sequence immobilized to a particular micro-array address, and further wherein the sampling position of the micro-array is such that the source light impinging on at least one micro-array address is substantially directed onto at least one detector pixel of the electronic light detector having a pixel address that is correlated to the micro-array address.

25

18. The system of claim 17, wherein the micro-array address to detector pixel address correlation is one-to-one, whereby the light impinging on a single micro-array address is directed to substantially one detector pixel.

30 19. The system of claim 17, wherein more than one detector pixel address is correlated to

one micro-array address.

20. The system of claim 1, wherein the light representative of the biological sample comprises light provided by at least one of chemi-luminescence, fluorescence, chemi-fluorescence, photon excitation, and a quenching thereof.

5 21. The system of claim 1, wherein the length of the light path between the biological sample and the plurality of detector pixels is in the range of 4 cm and 8 cm.

10 22. A polynucleic acid micro-array comprising a biological material holding structure having a sample surface and an opposing surface joined to the sample surface by a body portion, wherein the sample surface has immobilized nucleic acid sequences thereon, and further wherein the biological material holding structure is made of an opaque material.

15 23. A method for use in detecting biological material, the method comprising:
providing a biological sample in a sampling position, wherein the biological sample comprises biological material associated with a biological material holding structure, the biological holding structure having first and second opposing sides;
positioning an imaging device in proximity to the biological sample, wherein the imaging device comprises an electronic light detector array, wherein the electronic light detector array comprises a plurality of detector pixels located at particular detector pixel addresses, and further wherein the imaging device is positioned such that the plurality of detector pixels are facing the first side of the biological sample;

20 25 providing source light impinging on at least a portion of the first side of the biological material holding structure of the biological sample such that, in response to such impinging light, light representative of the biological sample is provided via a light path for detection by one or more of the detector pixels; and

30 acquiring at least one frame of image data representative of biological material of the biological sample using the plurality of detector pixels to detect the light representative of the biological sample provided via the light path.

24. The method of claim 23, wherein acquiring the at least one frame of image data comprises acquiring a plurality of frames of image data representative of biological material of the biological sample using the plurality of detector pixels, and further wherein the method comprises combining the plurality of frames of image data.

5

25. The method of claim 23, wherein providing source light comprises providing an excitation light that impinges on the at least one portion of the first side of the biological material holding structure of the biological sample such that, in response to the excitation light, fluorescence representative of biological material of the biological sample is provided via the light path for detection by one or more of the plurality of detector pixels, and further wherein acquiring the at least one frame of image data comprises acquiring at least one frame of image data representative of detected fluorescence.

10

26. The method of claim 25, wherein the light path of the fluorescence to one or more of the detector pixels does not include any portion of the biological material holding structure.

15

27. The method of claim 25, wherein the first side of the biological material holding structure comprises a sample surface having biological material thereon, and further wherein the sample surface is facing the plurality of detector pixels.

20

28. The method of claim 25, wherein providing the imaging device further comprises preventing excitation light from impinging on the plurality of detector pixels.

25

29. The method of claim 25, wherein providing the imaging device further comprises focusing the fluorescence onto one or more of the plurality of detector pixels.

30. The method of claim 25, wherein the biological material holding structure comprises an opaque material.

30

31. The method of claim 25, wherein the light path of the fluorescence to one or more of the

detector pixels includes at least a portion of the biological material holding structure.

32. The method of claim 25, wherein the biological sample is one of a micro-array and a gel, and further wherein one or more portions of the biological material of the biological sample comprises fluorescent markers.

33. The method of claim 23, wherein, in response to such impinging light, reflected light representative of the biological sample is provided via the light path for detection by one or more of the plurality of detector pixels, and further wherein acquiring the at least one frame of image data comprises acquiring at least one frame of image data representative of detected reflected light.

34. The method of claim 33, wherein the first side of the biological material holding structure comprises a sample surface having biological material thereon, and further wherein the sample surface is facing the plurality of detector pixels.

35. The method of claim 33, wherein the method further comprises focusing the reflected light onto one or more of the plurality of detector pixels.

36. The method of claim 33, wherein the biological holding material structure comprises an opaque material.

37. The method of claim 33, wherein the biological sample is one of a micro-array and a gel.

38. The method of claim 23, wherein the first side of the biological sample comprises a sample surface of a micro-array having one or more sequences of nucleic acids immobilized thereto, each sequence immobilized to a particular micro-array address, and further wherein the sampling position of the micro-array is such that the source light impinging on at least one micro-array address is substantially directed onto at least one detector pixel of the electronic light detector having a detector pixel address that is correlated to the micro-array address.

39. The method of claim 38, wherein the micro-array address to detector pixel address correlation is one-to-one, whereby the light impinging on a single micro-array address is directed to substantially one detector pixel.

5 40. The method of claim 38, wherein more than one detector pixel address is correlated to one micro-array address.

41. The method of claim 23, wherein the length of the light path between the biological sample and the plurality of detector pixels is in the range of 4 cm and 8 cm.

10 42. A method for detecting spots of polynucleic acid on a polynucleic acid chip, the method comprising:

15 providing a polynucleic acid chip in a holder at a sampling position, the polynucleic acid chip having a sample surface with one or more polynucleic acid sequences thereon, the sampling position being a position wherein the sample surface is facing a plurality of detector pixels of an electronic light detector array;

20 impinging source light on the sample surface to cause light to emanate from at least portions of the sample surface along a light path between the sample surface and the detector pixels; and

25 detecting the light emanating from the at least portions of the sample surface using one or more of the plurality of detector pixels.

43. The method of claim 42, wherein impinging source light on the sample surface comprises providing an excitation light that impinges on the at least one portion of the sample surface such that, in response to the excitation light, fluorescence representative of one or more polynucleic acid sequences is provided via the light path for detection by the one or more detector pixels.

44. The method of claim 43, wherein the light path of the fluorescence to one or more of the detector pixels does not include any portion of the polynucleic acid chip.

45. The method of claim 43, wherein the method further comprises preventing excitation light from impinging on the one or more detector pixels.

5 46. The method of claim 43, wherein the method further comprises focusing the fluorescence onto one or more of the detector pixels.

47. The method of claim 42, wherein the polynucleic acid chip is formed of an opaque material.

10 48. The method of claim 42, wherein the light path is less than 6 millimeters.

49. A system for detecting a pattern of polynucleic acid hybridization to a surface, the system comprising:

15 positioning structure to provide a polynucleic acid chip at a sampling position, the polynucleic acid chip comprising a sample surface and an opposing surface, the sample surface having one or more sequences of polynucleic acids immobilized thereto with each sequence being immobilized to a particular chip address;

20 an electronic light detector array, the electronic light detector array comprising detector pixels, the detector pixels being located at particular detector pixel addresses; and

25 a light source that provides source light, wherein the sampling position is a position that places the sample surface of the polynucleic acid chip in a defined spatial relationship relative to the electronic light detector array such that the source light impinging on at least one chip address on the sample surface is substantially directed onto at least one detector pixel with a detector pixel address that is correlated to the at least one chip address.

50. The system of claim 49, wherein the chip address to detector pixel address correlation is one-to-one, whereby the light impinging on a single chip address is directed to substantially one detector pixel address.

30 51. The system of claim 49, wherein more than one detector pixel address is correlated to

one chip address.

52. The system of claim 49, wherein light leaving the sample surface of the polynucleic acid chip passes through a thickness of the polynucleic acid chip before reaching the detector pixels.

5

53. The system of claim 49, wherein the polynucleic acid chip is formed of a light-transmissive material.

10 54. The system of claim 49, wherein the polynucleic acid chip comprises an optical filter that selectively transmits light.

15 55. The system of claim 49, wherein the system further comprises an optical filter that selectively transmits light.

20 56. The system of claim 55, wherein light leaving the sample surface of the polynucleic acid chip passes through the optical filter, wherein the optical filter is located between the sample surface and the detector pixels.

25 57. The system of claim 56, wherein the system further comprises a mapping lens that changes the direction of light rays leaving the sample surface of the polynucleic acid chip, wherein the mapping lens is located between the sample surface and the detector pixels.

58. The system of claim 57, wherein the mapping lens is one of a reducing lens and a magnifying lens.

25

59. The system of claim 57, wherein the mapping lens comprises means for collimating the light.

30

60. The system of claim 57, wherein the mapping lens and the optical filter are combined into a single lens/filter apparatus.

51. The system of claim 57, wherein the polynucleic acid chip comprises the mapping lens.

52. The system of claim 56, wherein the polynucleic acid chip is in direct physical contact with the filter.

5

53. The system of claim 62, wherein the opposing surface of the polynucleic acid chip is in direct physical contact with the filter.

10

54. The system of claim 62, wherein the sample surface of the polynucleic acid chip is in direct physical contact with the filter.

55. The system of claim 56, wherein the filter and the detector pixels of the detector array are in direct physical contact.

56. The system of claim 49, wherein the polynucleic acid chip and the electronic light detector array are in direct physical contact.

PCT/US2015/042640
2015
2016
2017
2018
2019
2020

57. The system of claim 66, wherein the sample surface of the polynucleic acid chip is in direct physical contact with the detector pixels of the electronic light detector array.

20
25

58. The system of claim 66, wherein the opposing surface of the polynucleic acid chip is in direct physical contact with the detector pixels of the electronic light detector array.

59. The system of claim 66, wherein all wavelengths of light that impinge on the sample 25 surface of the polynucleic acid chip are allowed to pass to the electronic detector array.

30

60. The system of claim 49, wherein a polynucleic acid dark spot is located on the sample surface, wherein the polynucleic acid dark spot is a spot that substantially blocks the passage of light, and further wherein the polynucleic acid dark spot is mapped onto the electronic light detector array.

71. The system of claim 70, wherein the light source is used to illuminate the sample surface so that light leaving the sample surface is projected onto the electronic light detector array such that the polynucleic acid dark spot on the sample surface which blocks more light than surrounding portions of the sample surface causes less light to be received by at least one detector pixel such that the polynucleic acid dark spot is detected.

5

72. A device for detecting a pattern of polynucleic acid hybridization on a surface, the device comprising:

10 providing a polynucleic acid chip at a sampling position, the polynucleic acid chip comprising a sample surface and an opposing surface, the sample surface having one or more sequences of polynucleic acids immobilized thereto with each sequence being immobilized to a particular chip address; and

15 an electronic light detector array, the detector array comprising detector pixels located at particular detector pixel addresses, wherein the sampling position places the sample surface of the polynucleic acid chip in a defined spatial relationship relative to the electronic light detector array such that light leaving a chip address is substantially directed onto at least one detector pixel with a detector pixel address that is correlated to a chip address.

20 73. The device of claim 72, wherein the chip address to detector pixel address correlation is one-to-one, whereby the light from a single chip address is directed to substantially one detector pixel address.

25 74. The device of claim 72, wherein more than one detector pixel address is correlated to one chip address.

75. The device of claim 72, wherein light leaving the chip address of the polynucleic acid chip passes through a thickness of the polynucleic acid chip before reaching the detector pixels.

30 76. The device of claim 75, wherein the polynucleic acid chip is formed of a light-transmissive material.

77. The device of claim 72, wherein a single optical lens is used to map an image of the sample surface onto the electronic light detector array.

5 78. The device of claim 72, wherein a plurality of optical lenses are used to map an image of the sample surface onto the electronic light detector array.

10 79. The device of claim 72, wherein the light leaving a chip address of the polynucleic acid chip is generated by one of chemiluminescence, fluorescence, two-photon excitation, multi-photon excitation, and quenching of fluorescence by polynucleic acids that attach to the sample surface.

15 80. The device of claim 72, wherein the light leaving a chip address is generated by a light source that generates source light.

20 81. The device of claim 80, wherein the light leaving a chip address is generated by a light source that generates source light and polynucleic acids that attach to the sample surface which have attached molecules that cause a decrease of the intensity of the light that leaves the sample surface.

25 82. The device of claim 72, wherein the light leaving a chip address of the polynucleic acid chip passes through an optical filter that allows substantially only light generated at the sample surface to pass to the detector.

83. The device of claim 72, wherein the polynucleic acid chip and the detector pixels of the electronic light detector array are in direct physical contact.

30 84. The device of claim 83, wherein the length of the light path is between 15 microns and 1 centimeter.

85. A system for imaging spots of polynucleic acid on a polynucleic acid chip, the system

comprising:

light source means for providing source light;

light detector means for detecting light, the light detector means comprising a plurality of detector pixels;

holding means for holding the polynucleic acid chip in a sampling position, wherein the polynucleic acid chip comprises a sample surface and an opposing surface, wherein the sample surface comprises chip addresses, and further wherein the sampling position places the sample surface in a defined spacial relationship relative to the light detector means such that light resulting from the source light impinging on at least one chip address travels a light path defined between the sample surface and the plurality of detector pixels and is mapped onto at least one detector pixel that is correlated with the at least one chip address; and

processing means for processing data from the light detector means.

86. The system of claim 85, wherein every point of the light path has an index of refraction that is greater than 1.0.

87. The system of claim 86, wherein the light path is comprised of solid materials.

88. The system of claim 85, wherein the light path does not include an optical lens that magnifies or reduces an image of the sample surface.

89. The system of claim 85, wherein the light path is less than one centimeter.

90. The system of claim 89, wherein the light path is less than one millimeter.

91. The system of claim 90, wherein the light path is less than 200 microns.

92. The system of claim 91, wherein the light path is less than 75 microns.

93. The system of claim 92, wherein the light path is less than 35 microns.

94. The system of claim 93, wherein the light path is less than 15 microns.

95. A polynucleic acid chip comprising:

a sample surface that has immobilized polynucleic acid sequences attached thereto; and
5 an opposed surface, wherein the chip is formed of a light transmitting material.

96. The chip of claim 95, wherein the chip comprises an optical filter.

97. The chip of claim 96, wherein the optical filter comprises an optical coating on the
10 opposed surface of the chip.

98. The chip of claim 97, wherein the optical coating allows passage of light wavelengths of fluorescence but substantially blocks other light wavelengths in the range of 300 nanometers to 600 nanometers.

15 99. The chip of claim 96, wherein the chip comprises an optical lens.

100. The chip of claim 95, wherein the chip comprises an optical lens.

101. The chip of claim 100, wherein the focal length of the optical lens is in the range of 10 microns to 750 microns.

102. The chip of claim 101, wherein the focal length of the optical lens is in the range of 10 microns to 400 microns.

25 103. The chip of claim 102, wherein the focal length of the optical lens is in the range of 10 microns to 250 microns.

104. The chip of claim 100, wherein the focal length of the optical lens is in the range of 5
30 microns to 40 microns.

105. A method for detecting spots of polynucleic acid on a polynucleic acid chip having a sample surface, the method comprising:

positioning the polynucleic acid chip at a sampling position, the sampling position being a position relative to an electronic light detector that establishes a light path distance between the sample surface and one or more detector pixels of the electronic light detector such that light emanating from one or more portions of the sample surface of the polynucleic acid chip travels along a light path to the one or more detector pixels of the electronic light detector; and

sensing the light emanating from one or more portions of the sample surface to detect the spots of polynucleic acid.

10

106. The method of claim 105, wherein the light path is less than four millimeters.

107. The method of claim 106, wherein the light path is less than 200 microns.

108. The method of claim 105, wherein the light path is substantially linear.

109. The method of claim 105, wherein providing the polynucleic acid chip in the sampling position comprises loading the polynucleic acid chip in a holder and moving the holder from a loading position into the sampling position.

110. The method of claim 109, wherein moving the holder from a loading position into a sampling position comprises sliding the holder from a loading position into a sampling position.

20

111. The method of claim 105, further comprising focusing an image representative of the detected spots of polynucleic acid, wherein such focusing comprises moving the holder to one or more other sampling positions until a sampling distance desired by a user is achieved.

112. The method of claim 111, wherein such focusing is automatically performed using a programmable computer.

25
30

113. A system for detecting a biological material of a biological sample, the system comprising:

positioning structure to provide a biological sample at a sampling position, wherein the biological sample comprises biological material associated with a biological material holding structure, the biological material holding structure having first and second opposing sides;

5 an electronic light detector array, wherein the electronic light detector array comprises detector pixels located at particular detector pixel addresses, and further wherein the detector pixels face the second side of the biological material holding structure; and

10 a bundled fiber optic light source apparatus, wherein the bundled fiber optic light source apparatus comprises:

a light source for providing source light,

15 a fiber bundle portion having a receiving end operable to receive source light from the light source, and

20 a fiber distribution array portion terminating the fiber bundle portion such that source light is provided from a linear array of fibers and impinges on at least one portion of the first side of the biological material holding structure, and further such that, in response to such impinging light, light representative of the biological sample is provided via a light path for detection by one or more of the detector pixels; and

25 control circuitry operable to control the scanning of the biological sample using the fiber optic bundle light source apparatus and the electronic light detector array to detect light representative of biological material of the biological sample such that multiple linear image portions of the biological sample are acquired.

114. The system of claim 113, wherein the biological material holding structure is light transmissive.

115. The system of claim 113, wherein the system further comprises movement structure to provide for scanning movement of at least one of the fiber optic bundle light source apparatus and the biological sample.